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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,909	10/13/2005	Yingxian Xiao	132848-01US	6970
50659 7590 11/05/2009				
BUTZEL LONG				
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EXAMINER				
ZARA, JANE J				
ART UNIT				
PAPER NUMBER				
1635				
NOTIFICATION DATE				
DELIVERY MODE				
11/05/2009				
ELECTRONIC				

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patent@butzel.com  
boudrie@butzel.com

### Office Action Summary

**Application No.**

10/552,909

**Applicant(s)**

XIAO ET AL.

**Examiner**

Jane Zara

**Art Unit**

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 July 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 11 and 21-33 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 11, 21-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Office action is in response to the communication filed 7-9-09.

Claims 1-5, 11, 21-33 are pending in the instant application.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

Applicant's arguments with respect to claims 1-5 and 11 have been considered but are moot in view of the new ground(s) of rejection set forth below.

#### **Rejections Necessitated by Amendments**

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 11, 21-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson (USPN 5,902,880) and Jennings et al, the combination in view of Fire et al (USPN 6,506,559), Tuschl et al (WO 02/44321) and Moyer et al (US 2005/0014263).

The claims are drawn to recombinant DNA constructs comprising at least one transcriptional unit comprising an engineered or native Type I Pol III transcriptional promoter, optionally one or more essential elements thereof, and further comprising a template for making an siRNA molecule with self-complementary strands between 17-23 nucleotides in length and optionally further comprising a spacer of 4-15 thymidines, and a transcriptional terminator optionally comprising at least five thymidines.

Thompson (USPN 5,902,880) teaches recombinant DNA constructs including cloning expression vectors comprising at least one transcriptional unit comprising an engineered or native Type I Pol III transcriptional promoter, or one or more essential elements thereof, and further comprising a template for making an RNA molecule, and a transcriptional terminator (see esp. col. 1-3, 7-10, claims 1, 2, 11, 19 and 21).

Jennings et al (EMBO J., Vol. 6, No. 10, pages 3043-3047, 1987) teach recombinant DNA constructs including cloning expression vectors comprising at least one transcriptional unit comprising an engineered or native Type I Pol III transcriptional promoter, or one or more essential elements thereof, and further comprising a template for making an RNA molecule, and a transcriptional terminator (see the abstract and introduction, page 3043, discussion on pages 3045-6).

The primary references of Thompson and Jennings do not teach expression vectors encoding siRNA molecules with self-complementary strands between 17-23 nucleotides in length and optionally further comprising a spacer of 4-15 thymidines, and a transcriptional terminator optionally comprising at least five thymidines.

Fire et al (USPN 6,506,559) teach siRNA molecules for targeting and inhibiting a target gene of known sequence. Fire teaches expression vectors encoding siRNA molecules and comprising an appropriate promoter which drives expression of the siRNA, which siRNA molecules are optionally expressed as a single, self-complementary strand (comprising a loop sequence between the sense and antisense strands) (see entire document, esp. col. 3, 4, 7-9; claim 21).

Tuschl et al (WO 02/44321) teach siRNA constructs comprising self-complementary strands between 17-23 nucleotides in length and which target and specifically hybridize to a known target gene sequence, which optionally comprise terminal overhangs comprising thymidines at the 3' termini (see entire document, esp. pages 2-5, 7, 19-22, 25, 33-34, 37, 43-45, 47-51).

Moyer et al (US 2005/0014263) teach expression constructs for introducing to mammalian host cells comprising appropriate promoter elements and further comprising transcriptional termination signals comprising at least 5 thymidine residues (see esp. paragraphs 0077-0078).

It would have been obvious to design and utilize recombinant expression constructs comprising a native or engineered Type I Pol III transcriptional promoter for driving expression of siRNA molecules because recombinant expression constructs

comprising this promoter were well known in the art, as taught previously by Thompson and Jennings, and the advantages of stability and cellular localization of inhibitory constructs in a host cell using the Type I Pol III promoter were taught by Jennings. One would have been motivated to express siRNA molecules using this expression construct, and as a single, self-complementary construct because siRNA molecules were well known in the art to act as efficient inhibitors of target gene expression and Fire taught the advantages of siRNA in target gene inhibition compared to other inhibitory constructs, and Fire also taught the expression of siRNA as a single, self-complementary construct in an appropriate expression vector. One would have been motivated to design an siRNA construct comprising intervening thymidine sequences because Tuschl and others in the art taught the advantages of including TT overhangs, especially at the 3' termini, in siRNA molecules used for target gene inhibition. One would have been motivated to include the well known transcriptional termination sequence comprising 5 thymidines because this termination sequence was well known in the art for use in vectors to drive expression of operably linked genes in recombinant expression vectors upon delivery to mammalian cells, as taught previously by Moyer et al. One of skill in the art would have reasonably expected that the instantly claimed expression constructs would provide efficient expression of self-assembling siRNA molecules upon delivery to target cells, and thereby provide for effective target gene inhibition in those target cells cell upon delivery and expression of the siRNA molecules.

For these reasons, the instant invention would have been obvious to one of ordinary skill at the time of filing the instant application.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore, can be reached on (571) 272-2914. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**Jane Zara**  
**11-2-09**

/Jane Zara/

Primary Examiner, Art Unit 1635